

**REMARKS**

Claims 54-78 were pending in this application when last examined. Claims 1-53 were previously cancelled. Non-elected claims 54-64, 67, 71 and 72 have been withdrawn.

Claims 54, 55, 57, 58, 64-66, 68, 69, 75-78 have been amended. Support for the amendments can be found in the specification at least at page 1, line 11; page 6, lines 12-13; and page 6, lines 32-34, and in the original claims as files. No new matter has been added.

**I. CLAIM OBJECTIONS**

At page 4, item 6, the Office Action objects to claims 65 and 75 for various informalities. Amended claims 65 and 75 address the informalities. In particular, amended claim 65 spells out indomethacin (INDO). Amended claim 75, as well as withdrawn amended claim 64, spells out blood-brain barrier. In addition, amended claim 75 corrects grammatical issues. Thus, Applicant requests reconsideration and withdrawal of the claim objections.

**II. CLAIM REJECTIONS - 35 USC § 112, FIRST PARAGRAPH**

At page 4, item 9, the Office Action rejects claim 76 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Office Action points specifically to the term "vector" and states that there is no

written support for a vector. Applicant respectfully traverses the rejection.

Amended claim 76 is directed to a composition comprising a pharmaceutically acceptable "carrier." Support for such a composition and carrier can be found in the specification at least at page 6, lines 12-13. Applicant requests reconsideration and withdrawal of the rejection.

**III. CLAIM REJECTIONS - 35 USC § 112, SECOND PARAGRAPH**

At page 5, item 11, the Office Action rejects claims 65, 66, 68-70, and 73-78 under 35 U.S.C. § 112, second paragraph, as being indefinite. The Office Action points specifically to the limitation "derivatives thereof" and states that the specification does not provide any structure or guidance to demonstrate what is meant by derivative. Applicant respectfully traverses the rejection.

Amended claims 65, 66, 68-70, 77 and 78, as well as withdrawn and amended claims 54, 55, 57, 58 do not recite the "derivatives" feature. Each of claims 65, 66, 68-70, and 73-78 clearly defines the intended subject matter, and each claim satisfies the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, Applicant requests reconsideration and withdrawal of the rejection.

#### IV. CLAIM REJECTIONS - 35 USC § 102

At page 6, item 13, the Office Action rejects claims 65, 68, 73, 74 and 77 under 35 U.S.C. § 102(b) as anticipated by Regtop et al. (US Patent No. 5,466,824). Applicant respectfully traverses the rejection.

Independent claim 65 is directed to a pharmaceutical composition comprising indomethacin (INDO) and/or salts thereof in combination with pharmaceutically effective amounts of at least one compound comprising metals and corresponding salts (or other non-elected species). Independent claim 77 is directed to a pharmaceutical composition comprising INDO in combination with a pharmaceutically effective amount of at least one metal and/or corresponding salt. Regtop fails to teach or suggest such compositions.

Regtop describes a complex of indomethacin, a divalent metal, and a tertiary or cyclic tertiary amide. The complex is defined as  $[M]_2[indomethacin]_4[S]_n$ , wherein M is the divalent metal, S is a molecule of a tertiary or cyclic tertiary amide, and n is 2 or 3. The complex is formed by dissolving indomethacin and a salt of the divalent metal in a tertiary amide, and adding a C<sub>1-4</sub> alkanol or C<sub>3-6</sub> ketone to the solution to precipitate the complex (see, Abstract). Regtop describes the potential use of copper, zinc, cobalt or nickel salts as the divalent metal salt, but discloses most preferably cupric acetate monohydrate (see, column 3, lines 2-5, and column 4, lines 19-21). Regtop prefers

copper<sub>2</sub>indomethacin<sub>4</sub> complexes, because of increased half-life compared to copper<sub>1</sub>indomethacin<sub>2</sub>, and its potent analgesic effect (see, column 6, lines 35-43). The copper<sub>2</sub>indomethacin<sub>4</sub> complexes are also less toxic (see, column 6, lines 61-64). The teachings of Regtop, including all of the Examples, are limited to copper<sub>2</sub>indomethacin<sub>4</sub> complexes formed in combination with a tertiary amide (i.e., [M]<sub>2</sub>[indomethacin]<sub>4</sub>[S]<sub>n</sub>), for the purpose of analgesic and anti-inflammatory activities.

The Regtop compound forms a complex of divalent metal, indomethacin and a tertiary amide, i.e., one single chemical structure including the INDO, divalent metal, and tertiary amide. The object of forming such a complex is not to exploit any additional or different biological property of the metal, but to make the INDO physiologically available in a form having reduced side-effects on the gastric mucosa when administered orally. Therefore, Regtop teaches that not all metals can be used for the purposes disclosed, but only divalent metals, and essentially only copper.

In contrast to Regtop, the present invention features a metal that does not need to be in a particular oxidative state, since the two active ingredients are not intended to form a complex with each other, but on the contrary, form a combination of two independent active ingredients. Preferred metals of the present invention include zinc, gold, selenium, bismuth and cadmium. Most preferred are gold, selenium and bismuth. Common

oxidation states of gold include +1 (gold I) and +3 (gold III), while bismuth is only found at the oxidation states +3 and +5 (trivalent and pentavalent). Selenium can be divalent but can also have oxidation states of +6 and +4. Regtop, however, is limited to and requires a divalent metal (copper) and a tertiary amide formed into a complex (i.e.,  $[M]_2[indomethacin]_4[S]_n$ ). Regtop fails to teach or suggest any type pharmaceutical composition that does not include this type of copper-amide complex.

For at least these reasons, Regtop fails to teach or suggest, fails to anticipate, a pharmaceutical composition having the combination of elements recited in claim 65, in claims 68, 73 and 74 dependent thereon, and in claim 77. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection.

#### **V. CLAIM REJECTIONS - 35 USC § 103**

At pages 7-10, items 17, 21, 25 and 29, the Office Action rejects claims 69, 70, 75, 76 and 78 under 35 U.S.C. § 103(a). The Office Action rejects claims 69 and 70 as obvious over Regtop in view of Berge et al. (Journal of Pharmaceutical Sciences, 1977), rejects claim 75 as obvious over Regtop in view of Wilkinson (Goodman & Gilman's The Pharmaceutical Basis of Therapeutics 10<sup>th</sup> ed., Chapter 1: Pharmacokinetics, 2001), rejects claim 76 as obvious over Regtop in view of Engler (US

Patent No. 6,165,779), and rejects claim 78 as obvious over Regtop in view of Taylor et al. (US Patent No. 6,303,295). Applicant respectfully traverses each of these rejections.

Each of the rejected claims depends from claim 65, and all of the above rejections rely on Regtop as the primary reference. Thus, for at least the same reasons as provided in the comments above regarding the rejection under 35 U.S.C. § 102, Regtop fails to teach or suggest a pharmaceutical composition comprising indomethacin (INDO) and/or salts thereof in combination with pharmaceutically effective amounts of metals and corresponding salts. Each of the cited secondary references, alone or in any combination, fails to remedy the deficient teachings of Regtop. For at least this reason, Regtop, Berge, Wilkinson, Engler, and/or Taylor fail to teach or suggest, and would not have rendered obvious, claims 69, 70, 75, 76 and 78. Applicant requests reconsideration and withdrawal of the rejection.

Furthermore, and with regard to claim 78, the Office Action acknowledges that Redtop fails to teach or suggest a composition comprising gold, selenium, or bismuth, as featured in claim 78. The Office Action relies on Taylor to teach selenium in combination with INDO. Applicant respectfully disagrees with this conclusion.

Taylor describes a method for the identification of nucleotide sequences which encode selenoproteins. The Office

Action cites a portion within the background information of Taylor which states that dietary selenium (Se) is critical for proper immune function (Se supplementation increases immunoglobulin G synthesis, increased chemotactic responses in neutrophils, enhancement of T cell cytotoxicity and proliferation in response to mitogens and antigens, see, column 1, lines 47-54).

Taylor, like Regtop, fails to teach or suggest the combination of INDO with gold, selenium, or bismuth as an antiviral composition. Taylor fails to teach or suggest that a pharmaceutical composition comprising selenium could be used for the treatment of diseases such as SARS, hemorrhagic fevers, diseases caused by coronavirus, etc., as featured in claim 65. Taylor merely states that selenium is an essential micronutrient. One of ordinary skill in the art would fail to find any suggestion or motivation in Taylor to combine selenium with indomethacin, or to include selenium with the Regtop anti-inflammatory composition, in order to produce a composition for the treatment of viral diseases as recited in claim 65. The combination of Regtop and Taylor fail to teach or suggest that the combination of INDO with gold, selenium, and/or bismuth is an effective anti-viral drug.

For at least these reasons, Regtop and Taylor fail to teach or suggest, and would not have rendered obvious, the composition of claim 78. Applicant requests reconsideration and withdrawal of the rejection of claim 78.

**VI. CONCLUSION**

Applicant solicits entry of the above amendments and respectfully requests that a timely Notice of Allowance be issued in this case.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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